PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF DEFECTS IN THE INTERNATIONAL APPLICATION

(PCT Articles 3(4)(i) and 14(1) and Rule 28.1)

To:
European Patent Office
Postbus 5818
Patentlaan 2
NL-2280 HV Rijswijk
PAYS-BAS

in its capacity as receiving Office

Date of mailing (*day/month/year*)	
28 January 1998 (28.01.1998)	
International application No. PCT/EP97/05214	International filing date (*day/month/year*) 23 September 1997 (23.09.1997)
Applicant BAVARIAN NORDIC RESEARCH INSTITUTE A/S	

The International Bureau hereby calls the attention of the receiving Office to the defects in the international application, which are specified on the attached

☒ Annex A ☐ Annex B ☐ Annex C

Additional observations, if necessary:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer F. Gateau
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Form PCT/IB/313 (July 1992)

ANNEX A TO FORM PCT/IB/313

International Application No.
PCT/EP97/05214

The International Bureau has found the following defects in the international application:

1. As to **signature*** of the international application (Rules 4.15 and 90.4), the request:

   a. ☐ is not signed.

   b. ☐ is not signed by all the applicants.

   c. ☐ is not accompanied by the statement referred to in the check list in Box No. VIII of the request explaining the lack of the signature of an applicant for the designation of the United States of America.

   d. ☐ is signed by what appears to be an agent/common representative but

      ☐ the international application is not accompanied by a power of attorney appointing him.

      ☐ the power of attorney accompanying the international application is not signed by all the applicants.

   e. ☒ other *(specify)*:
   The name and title of the persons signing on behalf of Bavarian Nordic.., University Malaysia Sarawak and GSF-Forschungszentrum... are not indicated on the powers of attorney.

* All applicants must sign, including inventors if they are also applicants (e.g. where the United States of America is designated).

2. As to indications concerning the **applicant**, the request (Rules 4.4 and 4.5):

   a. ☐ does not properly indicate the applicant's name *(specify)*:

   b. ☐ does not indicate the applicant's address.

   c. ☐ does not properly indicate the applicant's address *(specify)*:

   d. ☐ does not indicate the applicant's nationality.

   e. ☐ does not indicate the applicant's residence.

   f. ☐ other *(specify)*:

3. As to the **language** of some parts of the international application (Rule 12.1):

   a. ☐ the request is not in (one of) the admitted language(s) which is (are): English, French, German

   b. ☐ the text matter of the drawings is not in (one of) the admitted language(s) which is (are): English, French, German

   c. ☐ the abstract is not in (one of) the admitted language(s) which is (are): English, French, German

4. The **title** of the invention:

   a. ☐ is not indicated in Box No. I of the request (Rule 4.1).

   b. ☐ is not indicated at the top of the first sheet of the description (Rule 5.1(a)).

   c. ☐ as appearing in Box No. I of the request is not identical with the title heading the description (Rule 5.1(a)).

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REC'D 15 JAN 1999
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
PCT 796-019/mr		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP97/05214	23/09/1997	24/09/1996
International Patent Classification (IPC) or national classification and IPC		
C12N15/86		
Applicant		
BAVARIAN NORDIC RESEARCH INSTITUTE A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/03/1998	13. 01. 99
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Vollbach, S Telephone No. (+49-89) 2399-8715

Form PCT/IPEA/409 (Cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP97/05214

I. Basis of th report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-19	as originally filed				

Claims, No.:

1-10	as received on	06/10/1998	with letter of	06/10/1998	

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-8
	No:	Claims	9,10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

1. Present claims 1-8 are new and inventive with regard to the documents cited in the search report, because a recombinant vector expressing antigens from each of the four dengue virus serotypes has not been disclosed or suggested (Article 33(2) and Article 33(3) PCT).

2. Claims 9 and 10 are new in accordance with Article 33(2) PCT but lack an inventive step for the following reasons:

The MVA vector is known to be very safe in vaccine formulations (see D1: Developments in Biology standardization, vol. 84, 1995, Sutter et al., and D2: Vaccines vol 95, Modern approaches to new vaccines, 1995), the antigenicity of the dengue virus antigens has also been reported (see e.g. D3: WO 90/01946). Thus a person skilled n the art being confronted with the problem of providing safe vaccine formulations for dengue virus infection, would use the MVA vector in order to express different dengue virus antigens. This can easily be carried out by the use of standard procedures. Present claims 9 and 10 do not contain any features which would render said claims inventive. Therefore said claims are inadmissible under Article 33(3) PCT.

3. For the assessment of the present claims 8 and 10 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

1. A recombinant MVA containing and capable of expressing DNA sequences encoding one or more antigens from each of the four dengue virus serotypes (type 1, 2, 3 and 4).

2. A recombinant MVA according to claim 1, wherein the dengue virus antigen is selected from preM, E and/or NS1 antigens.

3. A recombinant MVA according to claim 1 or 2, wherein the DNA sequences are inserted at the site of naturally occurring deletions within the MVA genome.

4. A recombinant MVA according to claims 1 to 3, wherein the DNA sequences encoding antigen is under transcriptional control of the vaccinia virus early/late promoter P7.5.

5. A vaccine containing at least one recombinant MVA according to claims 1 to 4, and a pharmaceutically acceptable carrier or diluent.

6. The recombinant MVA according to any one of the preceding claims 1 to 4 for the prevention and/or treatment of dengue virus infection.

7. The recombinant MVA according to any one of the preceding claims 1 to 4 for the preparation of a medicament for the prevention and/or the treatment of dengue virus infection.

8. A method for the treatment or prevention of dengue virus infection comprising administering to a living animal body, including a human, in need thereof a

therapeutically effective amount of a recombinant MVA according to claims 1 to 4, or a vaccine according to claim 5.

9. A vaccine comprising as a first component a recombinant MVA carrying and capable of expressing T7 RNA polymerase and as further components one or more recombinant DNA vectors each carrying at least one dengue virus antigen under transcriptional control of a T7 RNA polymerase promoter.

10. A method for the treatment or prevention of a dengue virus infection comprising inoculating a living animal body, including a human, in need thereof with the first and further components of a vaccine according to claim 9 either simultaneously or with a timelag but using the same inoculation site.